-This is a divisional of co-pending application Serial No. 09/580,794 filed May 30, 2000, which is a divisional of Serial No. 08/913,833, filed September 15, 1997, now issued as Patent No. 6,078,093, which is a §371 national application of PCT/EP97/00211 filed January 17, 1997, which claims priority under 35 USC §119 to EP 96 870081.5 filed June 25, 1996 and EP 96 870005.4 filed January 26, 1996.-

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At page 1, following the above inserted paragraph, please add the heading:

-BACKGROUND OF THE INVENTION-

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At page 2, line 16, please insert the heading:

-BRIEF SUMMARY OF THE INVENTION-

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At page 5, line 7, please insert the following headings and nine paragraphs:

-BRIEF DESCRIPTION OF THE FIGURES

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4/11/03 RAA

Figure 1A-1H: Natural and drug induced variability in the vicinity of codons 41, 50, 67-70, 74-75, 150, 181-184, 215 and 219 of the HIV RT gene. The most frequently observed wild-type sequence is shown in the top line. Naturally occurring variations are indicated below. Drug-induced variants are indicated in bold italics.

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Figure 2 A. Reactivities of the selected probes for codon 41 immobilized on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 4. Each strip is incubated with a biotinylated PCR fragment from the reference panel. The reference panel accession numbers are indicated in Table 4. For several probes multiple reference panel possibilities are available, but only one relevant accession number given each time. *: False

positive reactivities. On top of the strips, the amino acids at the relevant codon, as derived from the probe reactivity, is indicated.

Figure 2 B. Reactivities of the selected probes for codons 69-70 immobilized on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 4. Each strip is incubated with a biotinylated PCR fragment from the reference panel. The reference panel accession numbers are indicated in Table 4. For several probes multiple reference panel possibilities are available, but only one relevant accession number given each time. *: False positive reactivities. On top of the strips, the amino acids at the relevant codon, as derived from the probe reactivity, is indicated.

Figure 2 C. Reactivities of the selected probes for codons 74-75 immobilized on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 4. Each strip is incubated with a biotinylated PCR fragment from the reference panel. The reference panel accession numbers are indicated in Table 4. For several probes multiple reference panel possibilities are available, but only one relevant accession number given each time. On top of the strips, the amino acids at the relevant codon, as derived from the probe reactivity, is indicated.

Figure 2 D. Reactivities of the selected probes for codons 184 immobilized on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 4. Each strip is incubated with a biotinylated PCR fragment from the reference panel. The reference panel accession numbers are indicated in Table 4. For several probes multiple reference panel possibilities are available, but only one relevant accession number given each time. On top of the strips, the amino acids at the relevant codon, as derived from the probe reactivity, is indicated.

Figure 2 E. Reactivities of the selected probes for codons 215 immobilized on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 4. Each

strip is incubated with a biotinylated PCR fragment from the reference panel. The reference panel accession numbers are indicated in Table 4. For several probes multiple reference panel possibilities are available, but only one relevant accession number given each time. On top of the strips, the amino acids at the relevant codon, as derived from the probe reactivity, is indicated.

Figure 2 F. Reactivities of the selected probes for codons 219 immobilized on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 4. Each strip is incubated with a biotinylated PCR fragment from the reference panel. The reference panel accession numbers are indicated in Table 4. For several probes multiple reference panel possibilities are available, but only one relevant accession number given each time. On top of the strips, the amino acids at the relevant codon, as derived from the probe reactivity, is indicated.

Figure 3. Clinical and virological features detectable in three patient follow-up samples. All three patients were infected with a HIV-1 strain showing the M41-T69-K70-L74-V75-M184-F214-T215-K219 genotype (wild type pattern). ~~Top~~: Fluctuations between plasma HIV RNA copy numbers (■) and CD4 cell count (x) are given in function of time. The different treatment regimens and the period of treatment is indicated on top. ~~Middle~~: Changes that appeared during the treatment period and that could be scored by means of the LiPA probes are indicated, for patient 91007 at codon 41 and 215; for patient 94013 at codon 184; for patient 92021 at codon 70, 214, 215, 219. ~~Bottom:~~ Corresponding LiPA strips for a subset of the aa changes are shown. LiPA probes are indicated on the left, the aa interpretation is indicated at the right of each panel.

Figure 4. Reactivities of the selected probes for codons 151 and 181 on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 3. LiPA strips were incubated with sequence-confirmed PCR fragments, extracted and amplified from: a wild-type HIV-1 isolate (strip 1), a wild-type isolate with a polymorphism at codon 151 (strip 2) or 149 (strip 3), a multi-drug resistant HIV-1 isolate (strip 4) with no information about codon

181 and a non-nucleoside analogue treated HIV-1 isolate which remained wild-type at codon 151 (strip5).

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DETAILED DESCRIPTION OF THE INVENTION—

At page 18, line 29, through page 21, line 12, please delete the heading "FIGURE AND TABLE LEGENDS" and the text describing the drawings.

At page 23, please delete the paragraph at lines 9-27 and replace with the following:

For cDNA synthesis and PCR amplification, the RNA pellet was dissolved in 15 μl random primers (20 ng/μl, pdN_6, Pharmacia), prepared in DEPC-treated or HPLC grade water. After denaturation at 70°C for 10 minutes, 5 μl cDNA mix was added, composed of 4 μl 5x AMV-RT buffer (250mM Tris.HC1 pH 8.5, 100mM KC1, 30mM $MgCl_2$, 25 mM DTT), 0.4 μL 25mM dXTPs, 0.2 μl or 25U Ribonuclease Inhibitor (HPRI, Amersham), and 0.3 μl or 8U AMV-RT (Stratagene). CDNA synthesis occurred during the 90 minutes incubation at 42°C. The HIV RT gene was then amplified using the following reaction mixture. 5 μl cDNA, 4.5 μl 10x Taq buffer, 0.3 μl 25 mM dXTPs, 1 μl (10 pmol) of each PCR primer, 38 μl H_2O, and 0.2 μl (1 U) Taq. The primers for amplification had the following sequence: outer sense RT-9: 5' bio-GTACAGTATTAGTAGGACCTACACCTGTC 3' (SEQ ID NO 162); nested sense RT-1: 5' bio-CCAAAAGTTAAACAATGGCCATTGACAGA 3' (SEQ ID NO 163); nested antisense RT-4: 5' bio-AGTTCATAACCCATCCAAAG 3' (SEQ ID NO 164); and outer antisense primer RT-12: 5' bio-ATCAGGATGGAGTTCATAACCCATCCA 3' (SEQ ID NO 39). Annealing occurred at 57°C, extension at 72°C and denaturation at 94°C. Each step of the cycle took 1 minute, the outer PCR contained 40 cycles, the nested round 35. Nested round PCR products were analysed on agarose gel and only clearly visible amplification products were used in the LiPA procedure. Quantification of viral RNA was obtained with the HIV Monitor™test (Roche, Brussels, Belgium).

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